Amendments to the Specification:

Please amend the paragraph on page 3, lines 17, through page 11, line 30, beginning, "Specifically, the present invention provides:..." as follows:

--Specifically, the present invention provides:

<1> a pharmaceutical agent comprising a dipeptidyl peptidase IV inhibitor and a biguanide agent in combination;

<2> the pharmaceutical agent according to <1>, which enhances the effects of active circulating glucagon-like peptide-1 (GLP-1) and/or active circulating glucagon-like peptide-2 (GLP-2);

<3> a pharmaceutical agent that enhances the effects of active circulating GLP-2;

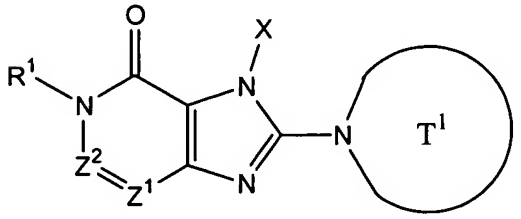
<4> a pharmaceutical agent comprising a dipeptidyl peptidase IV inhibitor and the pharmaceutical agent according to <3> in combination;

<5> the pharmaceutical agent according to <1> or <4>, wherein the dipeptidyl peptidase IV inhibitor is any one compound selected from:

(S)-1-((3-hydroxy-1-adamantyl)amino)acetyl-2-cyanopyrrolidine; (S)-1-(2-((5-cyanopyridin-2-yl)amino)ethyl-aminoacetyl)-2-cyanopyrrolidine; isoleucine thiazolidide; isoleucine pyrrolidide; and valine pyrrolidide;

or a salt or hydrate thereof;

<6> the pharmaceutical agent according to <1> or <4>, wherein the dipeptidyl peptidase IV inhibitor is a compound represented by the following formula, or a salt or hydrate thereof,



(I)

(wherein,

T^1 represents a monocyclic or bicyclic 4- to 12-membered heterocyclic group containing one or two nitrogen atoms in the ring, that may have one or more substituents;

X represents a C_{1-6} alkyl group which may have one or more substituents, a C_{2-6} alkenyl group which may have one or more substituents, a C_{2-6} alkynyl group which may have one or more substituents, a C_{6-10} aryl group which may have one or more substituents, a 5 to 10-membered heteroaryl group which may have one or more substituents, a C_{6-10} aryl C_{1-6} alkyl group which may have one or more substituents, or a 5 to 10-membered heteroaryl C_{1-6} alkyl group which may have one or more substituents;

Z^1 and Z^2 each independently represent a nitrogen atom or a group represented by the formula $-CR^2=$;

R^1 and R^2 each independently represent a group according to the formula $-A^0-A^1-A^2$

(wherein A^0 represents a single bond or a C_{1-6} alkylene group, which may have 1 to 3 substituents selected from group B consisting of the substituents described below;

A^1 represents a single bond, an oxygen atom, a sulfur atom, a sulfinyl group, a sulfonyl group, a carbonyl group, a group represented by the formula -O-CO-, a group represented by the formula -CO-O-, a group represented by the formula $-NR^A-$, a group represented by the formula $-CO-NR^A-$, a group represented by the formula $-NR^A-CO-$, a group represented by the formula $-SO_2-NR^A-$, or a group represented by the formula $-NR^A-SO_2-$;

A^2 and R^A each independently represent a hydrogen atom, a halogen atom, a cyano group, a C_{1-6} alkyl group, a C_{3-8} cycloalkyl group, a C_{2-6} alkenyl group, a C_{2-6} alkynyl group, C_{6-10} aryl group, a 5 to 10-membered heteroaryl group, a 4 to 8-membered heterocyclic group, a 5 to 10-membered heteroaryl C_{1-6} alkyl group, a C_{6-10} aryl C_{1-6} alkyl group, or a C_{2-7} alkylcarbonyl group;

however, A^2 and R^A each independently may have 1 to 3 substituents selected from the substituent group B described below:

when Z^2 is a group represented by the formula $-CR^2=$, R^1, and R^2 may in combination form a 5 to 7-membered ring;

except in cases where: [1] R^1 is a hydrogen atom; Z^1 is a nitrogen atom; and Z^2 is –CH=; and [2] Z^1 is a nitrogen atom; and Z^2 is -C(OH)=;

<Substituent group B>

Substituent group B represents the group consisting of: a hydroxyl group, a mercapto group, a cyano group, a nitro group, a halogen atom, a trifluoromethyl group, a C_{1-6} alkyl group which may have one or more substituents, a C_{3-8} cycloalkyl group, a C_{2-6} alkenyl group, a C_{2-6} alkynyl group, a C_{6-10} aryl group, a 5 to 10-membered heteroaryl group, a 4 to 8-membered heterocyclic group, a C_{1-6} alkoxy group, a C_{1-6} alkylthio group, a group represented by the formula $-SO_2-NR^{B1}-R^{B2}$, a group represented by the formula $-NR^{B1}-CO-R^{B2}$, a group represented by the formula $-NR^{B1}-R^{B2}$ (where R^{B1} and R^{B2} each independently represent a hydrogen atom or a C_{1-6} alkyl group), a group represented by the formula $-CO-R^{B3}$ (where R^{B3} represents a 4 to 8-membered heterocyclic group), a group represented by the formula $-CO-R^{B4}-R^{B5}$ and a group represented by the formula $-CH_2-CO-R^{B4}-R^{B5}$ (where R^{B4} represents a single bond, an oxygen atom, or a group represented by the formula $-NR^{B6}-$; R^{B5} and R^{B6} each independently represent a hydrogen atom, a C_{1-6} alkyl group, a C_{3-8} cycloalkyl group, a C_{2-6} alkenyl group, a C_{2-6} alkynyl group, a C_{6-10} aryl group, a 5 to 10-membered heteroaryl group, a 4 to 8-membered heterocyclic C_{1-6} alkyl group, a C_{6-10} aryl C_{1-6} alkyl group, or a 5 to 10-membered heteroaryl C_{1-6} alkyl group));

<7> the pharmaceutical agent according to <6>, wherein T^1 is a piperazin-1-yl group or a 3-amino-piperidin-1-yl group;

<8> the pharmaceutical agent according to <6>, wherein T^1 is a piperazin-1-yl group;

<9> the pharmaceutical agent according to any one of <6> to <8>, wherein X is a 3-methyl-2-buten-1-yl group, a 2-butynyl group, a benzyl group, or a 2-chlorophenyl group;

<10> the pharmaceutical agent according to any one of <6> to <8>, wherein X is a 3-methyl-2-buten-1-yl group or a 2-butyn-1-yl group;

<11> the pharmaceutical agent according to any one of <6> to <8>, wherein X is a 2-butyn-1-yl group;

<12> the pharmaceutical agent according to any one of <6> to <11>, wherein,

Z^1 is a nitrogen atom; and

Z^2 is a group represented by the formula [[$-CR_2=$]] $\underline{-CR^2=}$

(where R^2 is as defined in <6>);

<13> the pharmaceutical agent according to any one of <6> to <11>, wherein,

Z^2 is a nitrogen atom; and

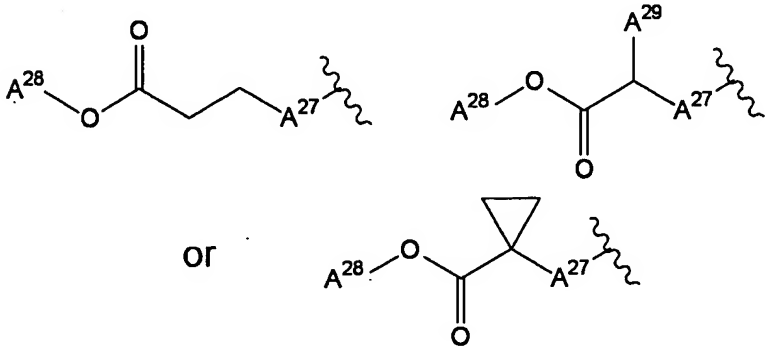
Z^1 is a group represented by the formula [[$-CR_2=$]] $\underline{-CR^2=}$

(where R^2 is as defined in <6>);

<14> the pharmaceutical agent according to any one of <6> to <13>, wherein R^1 is either a methyl group, a cyanobenzyl group, a fluorocyanobenzyl group, a phenethyl group, a 2-methoxyethyl group, or a 4-methoxycarbonylpridin-2-yl group;

<15> the pharmaceutical agent according to any one of <6> to <13>, wherein R^1 is a methyl group, or a 2-cyanobenzyl group;

<16> the pharmaceutical agent according to any one of <6> to <15>, wherein R^2 is either a hydrogen atom, a cyano group, a methoxy group, a carbamoylphenyloxy group, or a group represented by the formula:



(where,

A^{27} represents an oxygen atom, a sulfur atom, or -NH-;

A^{28} and A^{29} each independently represent a hydrogen atom or a C_{1-6} alkyl group);

<17> the pharmaceutical agent according to any one of <6> to <15>, wherein R^2 is a hydrogen atom, a cyano group, or a 2-carbamoylphenyloxy group;

<18> the pharmaceutical agent according to <6>, wherein the compound represented by formula (I) is any one compound selected from:

(1) 7-(2-butynyl)-2-cyano-1-methyl-8-(piperazin-1-yl)-1,7-dihydropurin-6-one;

(2) 3-(2-butynyl)-5-methyl-2-(piperazin-1-yl)-3,5-dihydroimidazo[4,5-d]pyridazin-4-one;

(3) 2-(3-aminopiperidin-1-yl)-3-(2-butynyl)-5-methyl-3,5-dihydroimidazo[4,5-d]pyridazin-4-one;

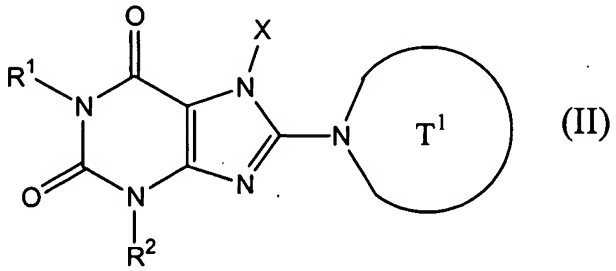
(4) 2-[7-(2-butynyl)-1-methyl-6-oxo-8-(piperazin-1-yl)-6,7-dihydro-1H-purin-2-yloxy] benzamide;

(5) 7-(2-butynyl)-1-(2-cyanobenzyl)-6-oxo-8-(piperazin-1-yl)-6,7-dihydro-1H-purine-2-carbonitrile; and

(6) 2-[3-(2-butynyl)-4-oxo-2-(piperazin-1-yl)-3,4-dihydroimidazo[4,5-d] pyridazin-5-ylmethyl] benzonitrile;

or a salt or hydrate thereof;

<19> the pharmaceutical agent according to <1> or <4>, wherein the dipeptidyl peptidase IV inhibitor is a compound represented by the following formula, or a salt or hydrate thereof,



(II)

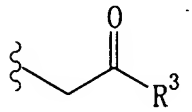
(wherein T^1, X, R^1, and R^2 are as defined in <6>);

<20> the pharmaceutical agent according to <19>, wherein T^1 is a piperazin-1-yl group;

<21> the pharmaceutical agent according to <19> or <20>, wherein X is a 2-butynyl group or a 2-chlorophenyl group;

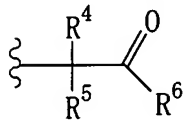
<22> the pharmaceutical agent according to <19> or <20>, wherein X is a 2-butynyl group;

<23> the pharmaceutical agent according to any one of <19> to <22>, wherein R^1 is a hydrogen atom, a methyl group, a 2-propynyl group, a 2-butynyl group, a cyanomethyl group, a phenethyl group, a phenoxyethyl group, or a group represented by the formula:



(where R^3 represents a hydroxyl group, a C_{1-6} alkoxy group, or a phenyl group);

<24> the pharmaceutical agent according to any one of <19> to <23>, wherein R^2 is a hydrogen atom, a C_{1-6} alkyl group, an ethoxyethyl group, a tetrahydrofuranylmethyl group, or a group represented by the formula:

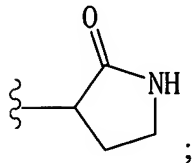


(where,

R^4 and R^5 are identical to or different from each other, and independently represent a hydrogen atom, a methyl group, or a phenyl group; and

R^6 represents a hydroxyl group, a C_{1-6} alkoxy group, or a phenyl group),

or a group represented by the formula:



;

<25> the pharmaceutical agent according to <19>, wherein the compound represented by formula (II) is any one compound selected from:

(1) 7-(2-butynyl)-1,3-dimethyl-8-(piperazin-1-yl)-3,7-dihydropurine-2,6-dione;

(2) 7-(2-butynyl)-3-methyl-8-(piperazin-1-yl)-3,7-dihydropurine-2,6-dione;

(3) methyl [7-(2-butynyl)-3-methyl-2,6-dioxo-8-(piperazin-1-yl)-2,3,6,7-tetrahydropurin-1-yl] acetate;

(4) 7-(2-butynyl)-3-methyl-8-(piperazin-1-yl)-1-(2-propynyl)-3,7-dihydropurine-2,6-dione;

(5) 1,7-bis(2-butynyl)-3-methyl-8-(piperazin-1-yl)-3,7-dihydropurine-2,6-dione;

(6) [7-(2-butynyl)-3-methyl-2,6-dioxo-8-(piperazin-1-yl)-2,3,6,7-tetrahydropurin-1-yl] acetonitrile;

(7) 7-(2-butynyl)-3-methyl-1-[(2-oxo-2-phenyl)ethyl]-8-(piperazin-1-yl)-3,7-dihydropurine-2,6-dione;

(8) 7-(2-butynyl)-3-ethyl-1-methyl-8-(piperazin-1-yl)-3,7-dihydropurine-2,6-dione;

(9) methyl [7-(2-butynyl)-1-methyl-2,6-dioxo-8-(piperazin-1-yl)-1,2,6,7-tetrahydropurin-3-yl] acetate;

(10) 7-(2-butynyl)-3-(2-tetrahydrofuranyl)methyl-1-methyl-8-(piperazin-1-yl)-3,7-dihydropurine-2,6-dione;

(11) methyl [7-(2-butynyl)-1-methyl-2,6-dioxo-8-(piperazin-1-yl)-1,2,6,7-tetrahydropurin-3-yl]phenylacetate;

(12) 7-(2-butynyl)-3-propyl-1-methyl-8-(piperazin-1-yl)-3,7-dihydropurine-2,6-dione;

(13) 7-(2-butynyl)-3-(2-oxo-2-phenethyl)-1-methyl-8-(piperazin-1-yl)-3,7-dihydropurine-2,6-dione;

(14) ethyl 2-[7-(2-butynyl)-1-methyl-2,6-dioxo-8-(piperazin-1-yl)-1,2,6,7-tetrahydropurin-3-yl] propionate;

(15) 7-(2-butynyl)-3-(2-ethoxyethyl)-1-methyl-8-(piperazin-1-yl)-3,7-dihydropurine-2,6-dione;

(16) 7-(2-butynyl)-3-isopropyl-1-methyl-8-(piperazin-1-yl)-3,7-dihydropurine-2,6-dione;

(17) 7-(2-butynyl)-3-(3,3-dimethyl-2-oxobutyl)-1-methyl-8-(piperazin-1-yl)-3,7-dihydropurine-2,6-dione;

(18) 7-(2-butynyl)-1-methyl-3-(2-oxopyrrolidin-3-yl)-8-(piperazin-1-yl)-3,7-dihydropurine-2,6-dione;

(19) 7-(2-butynyl)-3-(2-ethoxyethyl)-1-(2-oxo-2-phenylethyl)-8-(piperazin-1-yl)-3,7-dihydropurine-2,6-dione;

(20) methyl [7-(2-butynyl)-2,6-dioxo-1-(2-oxo-2-phenylethyl)-8-(piperazin-1-yl)-1,2,6,7-tetrahydropurin-3-yl] acetate;

(21) ethyl [7-(2-butynyl)-2,6-dioxo-1-(2-phenethyl)-8-(piperazin-1-yl)-1,2,6,7-tetrahydropurin-3-yl] acetate;

(22) [7-(2-butynyl)-2,6-dioxo-1-(2-phenethyl)-8-(piperazin-1-yl)-1,2,6,7-tetrahydropurin-3-yl] acetate;

(23) 7-(2-butynyl)-3-[2-oxo-2-(pyrrolidin-1-yl)ethyl]-1-(2-phenethyl)-8-(piperazin-1-yl)-3,7-dihydropurine-2,6-dione;

(24) 2-[7-(2-butynyl)-2,6-dioxo-1-(2-phenethyl)-8-(piperazin-1-yl)-1,2,6,7-tetrahydropurin-3-yl]-N-methylacetamide;

(25) 2-[7-(2-butynyl)-2,6-dioxo-1-(2-phenethyl)-8-(piperazin-1-yl)-1,2,6,7-tetrahydropurin-3-yl]-N-cyclopropyl acetamide;

(26) 2-[7-(2-butynyl)-2,6-dioxo-1-(2-phenethyl)-8-(piperazin-1-yl)-1,2,6,7-tetrahydropurin-3-yl]-N-phenylacetamide; and

(27) 2-[7-(2-butynyl)-2,6-dioxo-1-(2-phenethyl)-8-(piperazin-1-yl)-1,2,6,7-tetrahydropurin-3-yl]-N-(2-propynyl) acetamide;

or a salt or hydrate thereof;

<26> the pharmaceutical agent according to <1>, wherein the biguanide agent is metformin;

<27> the pharmaceutical agent according to <1> or <2>, which is a preventive or therapeutic agent for a disease which is associated with active circulating GLP-1 and/or active circulating GLP-2;

<28> the pharmaceutical agent according to <27>, wherein the disease is at least any one selected from the group consisting of: diabetes, obesity, hyperlipidemia, and gastrointestinal diseases;

<29> the pharmaceutical agent according to <3> or <4>, which is a preventive or therapeutic agent for a disease which is associated with active circulating GLP-2;

<30> the pharmaceutical agent according to <29>, wherein the disease is a gastrointestinal disease;

<31> a method for preventing or treating a disease which is associated with active circulating GLP-1 and/or active circulating GLP-2, which comprises administering the pharmaceutical agent according to <1> or <2> at an effective amount;

<32> the use of the pharmaceutical agent according to <1> or <2> for producing a preventive or therapeutic agent for a disease which is associated with active circulating GLP-1 and/or active circulating GLP-2;

<33> a method for preventing or treating a disease which is associated with active circulating GLP-2 , which comprises administering the pharmaceutical agent according to <3> or <4> at an effective amount;

<34> the use of the pharmaceutical agent according to <3> or <4> for producing a preventive or therapeutic agent for a disease which is associated with active circulating GLP-2;

<35> a method for enhancing the effects of active circulating GLP-1 and/or active circulating GLP-2, which comprises using the pharmaceutical agent according to <1> or <2>; and

<36> a method for enhancing the effects of active circulating GLP-2, which comprises using the pharmaceutical agent according to <3> or <4>.--

Please amend the heading on page 88, lines 24-25 as follows:

--[[(d) [7-(2-Chlorophenyl)-1-methyl-2,6-dioxo-1,2,6,7-tetrahydropurin-3-yl]methyl 2,2-dimethylopropionate]] (d) [7-(2-Chlorophenyl)-1-methyl-2,6-dioxo-1,2,6,7-tetrahydropurin-3-yl]methyl 2,2-dimethylpropionate --.

Please amend the paragraph on page 107, lines 5-11, beginning, "0.235 of trimethyl oxonium tetrafluoroborate was added to a 20-ml dichloromethane...", as follows:

--~~0.235~~ 0.235 g of trimethyl oxonium tetrafluoroborate was added to a 20-ml dichloromethane solution of 0.58 g of t-butyl 4-[1-(2-butynyl)-5-ethoxycarbonyl-4-thiocarbamoyl-1H-imidazol-2-yl]piperazine-1-carboxylate, and the mixture was stirred at room temperature for 18 hours. 50 ml of dichloromethane was added to the solution, and the mixture was washed with 20

ml of a saturated sodium bicarbonate solution. The mixture was dried over anhydrous magnesium sulfate, and concentrated under reduced pressure to give 0.55 g of the title compound.--.

Please amend the heading on page 124, lines 6-8 as follows:

--[[(f) t-Butyl [1-[7-(2-butynyl)-2-cyano-1-(2-cyanobenzyl)-6-oxo-6,7-dihydro-1-purin-8-yl]piperidin-3-yl]carbamate]] (f) t-Butyl [1-[7-(2-butynyl)-2-cyano-1-(2-cyanobenzyl)-6-oxo-6,7-dihydro-1H-purin-8-yl]piperidin-3-yl]carbamate --.

Please amend the heading for the compound found on page 175, second column, second compound from the top as follows:

--~~Example 1 (g) 2~~ Example 1 (g)-1--.